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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/975,317	10/12/2001	Alan David Watson	WATS3001/REF/C	8178

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EXAMINER

HARTLEY, MICHAEL G

ART UNIT

PAPER NUMBER

1616

DATE MAILED: 07/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/975,317

Applicant(s)

WATSON ET AL.

Examiner

Michael G. Hartley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 51-74 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 51-74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/17/2004 has been entered.

***Response to Amendment***

The amendment(s)/response(s) filed 3/17/2004; 4/30/2004 and 5/18/2004 have been entered.

***Response to Arguments***

Applicant's arguments with respect to claims 51-74 are have been considered but are moot in view of the new ground(s) of rejection.

Further, the explanation of the unexpected results for Mn over Gd is not found persuasive because the provided results are neither commensurate in scope with the pending claims nor are a comparison with the closest prior art. The presented articles, that compare Mn to Gd, are limited to the use of MnCl<sub>2</sub> and Mn-EDTA in methods using inversion recovery planer MRI, while the claims are neither limited to such chelates nor such methods. There is nothing to suggest that the results in these specific tests in the paper would hold true for the scope of the claimed invention. Also, these cited articles do not provide a comparison with the closest prior art, as Mn-chelates are known in the art for such methods, as shown below.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 51-53, 55-58 and 63-74 are rejected under 35 U.S.C. 102(b) as being anticipated by Rocklage (US 5,190,744).

Rocklage discloses a method of detecting myocardial ischemia in a subject comprising administering a contrast medium comprising a manganese complex and subjecting the subject to a fast MRI technique to detect abnormal blood flow, see abstract. Methods of fast MRI, as claimed, are disclosed in column 2, lines 10+ and manganese chelates are disclosed, see column 4, line 55 and claim 26. The dosages are within the claimed dosages, e.g., 0.1 to 0.4 mmol/kg, see column 5, lines 38+. The methods are for imaging myocardial ischemia, see columns 2 and 8. Rocklage discloses the use of the same contrast agents as claimed, e.g., DTPA, macrocyclics (DOTA), etc., see column 4. Since the same chelators are used, as encompassed by the instant claims, the metal complexes thereof would inherently be expected to have the same Pk values, as claimed. The contrast agents include pharmaceutical composition containing calcium complexes, buffers, antioxidants, etc., as claimed, see column 6.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 59-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rocklage (US 5,190,744) in view of Rocklage (US Pat. 4,889,931).

Rocklage '744 discloses a method of detecting myocardial ischemia in a subject comprising administering a contrast medium comprising a manganese complex and subjecting the subject to a fast MRI technique to detect abnormal blood flow, as set forth above.

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Rocklage '744 teaches that various known chelating agents may be employed in column 4, but fails to specifically disclose the use of the same contrast agents as instantly claimed (e.g., manganese complexes, such as, those of formula I (claim 55) and dosages thereof.

Rocklage '981 discloses MRI contrast agents comprising manganese are superior chelating agents which are highly stable, making them very suitable for methods of MRI imaging, see column 1. Rocklage '981 also teaches that manganese in the preferred metal for such MRI complexes. The contrast agents include manganese complexes of DPDP, etc. is especially preferred, see column 4, lines 50+. These chelates are the same as those instantly claimed and are used in dosages which encompass those instantly claimed, see column 9, lines 1+.

It would have been obvious to one of ordinary skill in the art to modify the methods disclosed by Rocklage '744 to use a manganese contrast agent and dosages thereof, as instantly claimed, because such Rocklage '981 teaches that such contrast agents (e.g., a manganese complex of DPDP, etc.) are superior chelating agents which are highly stable, thus, making them very suitable for methods of MRI imaging when used in dosages encompassed by the claims. One of ordinary skill in the art would have been motivated to employ the improved manganese complexes as the contrast agents in the methods of Rocklage '744 to gain the advantages Mn complexes, including optimum MRI properties, decreased toxicity, etc., as is known in the art, as shown by Rocklage '981.

#### ***Claim Rejections - 35 USC § 103***

Claim 54 rejected under 35 U.S.C. 103(a) as being unpatentable over Rocklage (US 5,190,744) in view of Goldenberg (US Pat. 5,632,968).

Rocklage '744 teaches that "various varieties of echo planer imaging (EPI) are particularly suitable" in column 2, lines 20-23, but fails to specifically disclose that the echo imaging is an inversion recovery echo imaging method.

Goldenberg discloses methods of imaging cardiovascular lesions and teaches that inversion recovery is a well known and equivalent method of spin-echo MRI, see column 13, lines 23-48.

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It would have been obvious to one of ordinary skill in the art to further modify the methods disclosed by Rocklage to use inversion-recovery spin-echo MRI as the spin echo MRI procedure because it is well known in the art that this is a useful and equivalent method of spin-echo MRI as taught by Goldenberg.

***Conclusion***

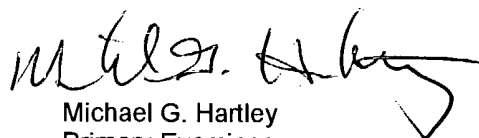
The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Gries US 4,957,939 and Meade US 5,707,605 are made of record for disclosing methods of imaging cardiac infarction using Mn-chelates as dosages as claimed, but was not cited herein as it was viewed as cumulative to the references relied upon hereinabove.

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (571) 272-0616. The examiner can normally be reached on M-Tu and Th-F, 7:30-4, Telework on Wed..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Michael G. Hartley  
Primary Examiner  
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